Return to NINDS Parkinson's Disease Research Web

Brain Banks & Other Repositories

Principal Investigator:
Grant Number: N01NS022349
Title: Genetic Resource Center

Abstract: Unavailable

Principal Investigator:
Grant Number: Y1NS800208
Title: Human Specimans Bank

Abstract: Unavailable

Principal Investigator: BENES, FRANCINE M
Grant Number: 5R24MH068855-02
Title: A National Resource for Postmortem Brain Research

Abstract: This is a competitive renewal application for the Harvard Brain Tissue Resource Center, a national resource for the acquisition, processing, storage and distribution of high quality postmortem (PM) brain to the neuroscience community. This facility collects brains from normal controls (CON), as well as individuals with a variety of movement disorders (Huntington's chorea and Parkinson's disease), dementias (Alzheimer's disease, frontotemporal dementias) and major psychoses (schizophrenia and bipolar disorders). The HBTRC distributes tissue specimens to neuroanatomists, neuropathologists, neuropharmacologists, neurochemists and molecular biologists throughout the U.S. Over the past 5 years, this tissue has contributed to more than 170 scientific publications. During the current funding period, the HBTRC has undergone a major restructuring that has resulted in an increase in the overall quality and efficiency of its operation. An important outcome of this re-organization has been an increase in the number of fresh, frozen cases and a marked decrease in the postmortem interval (PMI). As a result of this effort, abundant, high quality tissue is now available for a broad array of state-of-the-art research applications. The number of CONs received by the HBTRC has more than doubled during the current funding period and the HBTRC is now able to provide investigators with sets of CONs and diseased brains matched for age, PMI, gender and hemisphere. For the major psychoses, where the acquisition of postmortem brains is actually challenging, the number of schizophrenic and bipolar cases has also increased. Since these are largely from community-based referrals, the potential confounding effects of institutionalization, inanition and substance abuse are relatively lower than in medical examiner cases. To facilitate the donation process, the HBTRC has established a website with a) Informed Consent forms for potential donors and their families, b) instructions for handling brains by pathologists or dieners involved in brain removal, and c) application forms for investigators seeking tissue for their research. The HBTRC has also developed a User-Interactive Database, so that investigators who receive tissue from the "bank" can obtain demographics, neuropathology reports and images of gross dissections and histological slides for their cases. With supplemental funding from NIH, the HBTRC is now obtaining gene expression profiling and SNP analyses using the standard Affymetrix microarray system and this information will be immediately placed in our public domain National Databank as it is obtained. All investigators receiving tissue from the HBTRC will also be encouraged to "deposit" their findings in the Databank so that they will be available to the

Principal Investigator: DAWSON, TED M
Grant Number: 2P50NS038377-06A1
Title: Parkinson's Disease Research Center of Excellence

Abstract: The overall goals of this proposal are to understand the role of alpha-synuclein, parkin, DJ-1 and synphilin-1 in the pathogenesis and pathology of Parkinson's disease (PD) and to define the molecular mechanisms of neuronal injury in animal models of PD. The program represents a multi-disciplinary, mechanistic approach involving interactive, productive investigators with complementary areas of expertise who have long been committed to the studies of neurodegenerative diseases. Their aim will be to integrate the activities of various disciplines such that the interrelationships will result in a greater scientific contributions and achievements if each project were pursued individually. The program has one major theme: To understand the role of familial associated genes alpha-synuclein, parkin and DJ-1 in the pathogenesis of Parkinson's disease and related disorders. The role of alpha-synuclein, parkin, DJ-1 and synphilin- 1 in PD pathogenesis will be investigated using molecular, transgenic, neuropathologic, cell biologic and neurobehavioral approaches to examine the mechanism of neuronal dysfunction and injury clue to alterations in these gene products. The mechanism of neuronal loss in Parkin knockout mice and alpha-synuclein A53T transgenic mice will be characterized. We will determine whether parkin interacts with alpha-synuclein and further explore the relation between and parkin, alpha-synuclein and synphilin-1. We will explore alpha-synuclein processing and modifications and the relationship of synphilin-1 to alpha-synuclein. Furthermore, we will investigate the potential function of DJ-1 and it role in PD Pathogenesis. We believe that our multi-disciplinary approach has the capacity to produce unique information concerning the mechanisms of neurodegeneration in genetic animal models of Parkinson's disease and the related synucleinopathies and to lead to better understanding of the function and the role of alpha-synuclein, parkin, DJ-1 and synphilin-1 in normal and pathophysiologic processes related to PD. The program consists of four projects: 1) Mouse Models of Parkin Biology and Pathobiology 2) PD Cell Models: Alpha-synuclein and Interacting Proteins; 3) Mechanisms of Neurodegeneration in Human Alpha-synuclein Transgenic Mice; 4) The Role of DJ-1 in Parkinson's Disease and four cores A) Administration and Training; B) Transgenic and Neurobehavior; C) Neuropathology and D) Clinical.-

Principal Investigator: DICKSON, DENNIS W
Grant Number: 2P50NS040256-06
Title: Genetics and Molecular Biology of Parkinsonism

Abstract: The Udall Center for Excellence in Parkinson's Disease Research at the Mayo Clinic is an integrated, multidisciplinary center that studies the Genetics and Molecular Biology of Parkinsonism. The Center draws upon the clinical strengths of the Mayo Clinic Movement Disorder Section as well as epidemiologic and longitudinal studies of Parkinson's disease (PD), dementia with Lewy bodies and aging that provide clinical material for research projects. The Clinical Core is a multi-national effort to identify and characterize multiplex families with PD for genetic studies of PD. The Clinical Core also recruits and follows sporadic PD patients and arranges for postmortem studies. The Genetic Core provides genetic screening and performs genome wide linkage studies of familial PD. When permission is granted, samples are submitted to the NINDS DNA repository. The Neuropathology Core performs postmortem evaluations of PD, provides histologic support for projects and provides postmortem material collected through several different avenues for the research projects. Project 1 builds upon progress from the previous funding period demonstrating multiplication of the alpha-synuclein gene (SCNA) in autosomal dominant, early-onset PD and focuses on population genetics of SNCA, characterization of SNCA multiplications (including the size and genes within the multiplication regions), and measuring temporal and regional alpha-synuclein expression in normals and a-synucleinopathies. Project 2 is a clinicopathologic study that determines the frequency and clinical expression of Lewy bodies in normal individuals using the Mayo Medical Records Linkage System, with studies on the role of neuronal loss, inflammation and tau on clinical features. Project 3 uses cell lines that inducibly express alpha-synuclein as well as mitochondrial toxins, such as rotenone, to study truncated and aggregated alpha-synuclein with the goal of determining the role of interacting proteins in aggregate formation and the effects of aggregates on proteasome function and gene expression.-

Principal Investigator: KURLAN, ROGER M
Grant Number: 1U01NS050095-01
Title: Parkinson's Disease Data Organizing Center

Abstract: In response to RFA-NS-NS-05-001, we propose to establish a Parkinson's Disease Data Organizing Center (PD-DOC) at the University of Rochester. In keeping with the RFA, the PD-DOC will: 1) establish, maintain and disseminate a shared, central and standardized longitudinal database in support of the prospective collection and analysis of clinical, neuropathological and biologic data from patients with PD and controls, 2) assess and move toward the potential integration of relevant pre-existing databases, 3) assist investigators planning to perform research studies using the shared database, 4) prepare and maintain an up-to-date catalog of research materials at participating sites that might be used for PD research and, 5) coordinate annual meetings of the PD-DOC Steering Committee. The University of Rochester has extensive expertise and resources which will facilitate the development of a highly successful PD-DOC. The PD-DOC will be a critical force in advancing collaborative research in PD. -

Principal Investigator: LOUIS, ELAN D
Grant Number: 5R01NS042859-02
Title: Pathogenesis Of Essential Tremor: Cerebellar Metabolism

Abstract: Essential tremor (ET) is the most common tremor disorder, twenty times more prevalent than Parkinson's disease. Up to 6% of the general population has ET. Uncontrollable trembling eventually forces 10 - 25% of patients to retire prematurely. There is no cure, and few medications lessen the tremor, although deep brain stimulation has provided promising results. Clinical evidence and neuro-imaging studies suggest that the cerebellum is centrally involved in ET, and evidence from clinical and animal studies suggests that there may be a disturbance in the gamma amino butyric acid (GABA) neurotransmitter system. While ET is clinically progressive, little is known about its underlying pathology. There have been few published postmortem examinations. The fundamental question in ET research is whether an underlying pathology can be identified in terms of morphological or morphometric changes of specific cell types in specific brain regions? Second, is there a neurotransmitter abnormality in ET, either resulting as a consequence of cell loss or in the absence of cell loss? The proposed study will be a collaborative effort involving four centers in the United States and Canada where archival postmortem tissue on 24 ET patients is available. In addition, with the help of the International Essential Tremor Foundation, we will establish at Columbia University a centralized repository for new prospectively-collected ET brains, collecting 36 additional ET brains during the five-year period. The 60 ET brains will be compared with 40 control brains. Primary Aim 1 is to study the pathology of ET to determine whether there are changes in specific brain regions. Using conventional morphological methods and quantitative morphometric assessments (stereology), tissue will be examined for changes, including cell loss, in the main region of interest (cerebellar hemispheres) and in secondary regions of interest (red nuclei, thalami, inferior olivary nuclei). We hypothesize that changes and cell loss in the cerebellum will be present to a greater extent in ET than in control brains. Primary Aim 2 is to study the GABA neurotransmitter system. We hypothesize that there will be differences in cerebellar GABA-ergic immuno-labeling in ET compared to control brains. Current therapies for ET have come to us by serendipity and are ineffective in up to 50% of patients. Knowledge of the pathological changes and neurochemical abnormality in ET is critical for the design of new therapies for ET.-

Principal Investigator: Montine, Thomas J
Grant Number: 5R01NS048595-02
Title: Dementia with Lewy Bodies: A Collaborative Study

Abstract: Patients with the pathologic diagnosis of Alzheimer's disease (AD) commonly (approximately 30 to 60%) have concomitant Lewy body (LB) formation as detected with o_-synuclein immunohistochemical analysis of extra-nigral sites. These patients with AD/LB, along with a much less common dementia characterized by LB formation alone, are currently classified as having Dementia with Lewy Bodies (DLB). There is substantial clinical and pathologic heterogeneity among patients with DLB, thwarting efforts to understand fully the significance of distinguishing AD from DLB and strongly suggesting further distinct subgroups within what is currently called DLB. Here we propose to test the hypothesis that DLB differs from AD at clinical, pathologic, molecular genetic, and biochemical levels, and that these same criteria may be used to discem multiple distinct subgroups of DLB. We will expand an already functioning cooperative study among five Alzheimer Disease Centers (ADC) across the United States: Oregon Health & Science University, University of California at San Diego, University of Pennsylvania, University of Pittsburgh, and University of Washington. We propose to collect clinical and neuropathological data as well as banked tissue from approximately 100 age-matched controls, 250 patients with AD, and 250 patients with DLB. We estimate collection of 20, 50, and 50, respectively, additional cases for each year of this project. Using the robust design of patient data and material from five separate ADCs and biostatistical support from the National Alzheimer's Coordinating Center (NACC), we will test our hypothesis by pursuing these specific aims: to distinguish controls, AD, and DLB, and as well as DLB subgroups by determining (1) clinical and pathological features, (2) characteristics of candidate genes, (3) quantitative differences in oxidative damage, and (4) alterations in both soluble and insoluble forms of tan, A[3, and (z-synuclein. Successful completion of this project will solidify our understanding of DLB and provide a foundation for future clinical and molecular studies of this second most common form of dementia. Specifically, this project will establish a National DLB Resource, including a database of clinico-pathologic data, as well as an inventory of DNA samples and frozen brain tissue. This resource will be made available for future investigations of DLB.-

Principal Investigator: VAN DEERLIN, VIVIANNA
Grant Number: 5K08NS041408-04
Title: Tau Isoform Expression in FTDP-17

Abstract: Filamentous aggregates of hyperphosphorylated tau are the signature brain lesions of frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP 17), an inherited tauopathy with diverse, phenotypes caused by different tau gene mutations. Tau is a microtubule (MT) binding protein that promotes tubulin polymerization into MTs and stabilizes MTs. The adult human brain contains six tau isoforms, half with 3 3R isoforms) and half with 4 Cterminal MTbinding repeats (4R isoforms) generated by alternatively splicing of exon 10 (E 10). Tau gene mutations cause FTDP 17 by impairing E 10 alternative splicing or tau functions. A puzzling aspect of the FTDP 17 syndromes is that different tau mutations damage selected subtypes of neurons and glia. Our first hypothesis is that this selective vulnerability may reflect cell type specific perturbations of tau isoforms to cause varied phenotypes. To test this hypothesis, we will determine mRNA expression profiles of tau isoforms in normal brain cell subpopulations. Although the ratio of 3R to 4R tau is 1:1 in normal human brain, it has never been determined in subpopulations of neurons and glia. In, Aim 1, we will microdissect neurons and glia from paraffinembedded tissue sections of control brains, perform linear amplification on extracted RNA followed by quantitative realtime RTPCR to measure the relative levels of each tau isoform mRNA. In Aim 2, we will similarly study the same neuronal and glial cell populations in FTDP 17 brains. Correlation of these data with disease phenotypes will clarify mechanisms of FTDP1 7. Since FTDP1 7 mutations produce different phenotypes in the same kindred, a second hypothesis proposes that altered expression of a second gene, which interacts with the tau gene or protein, influences development of phenotypic manifestations of FTDP 17 in different affected family members. Aim 3 tests this hypothesis by examining the differential expression of candidate genes (i.e. those involved in splicing, RNA stability, tau function, other cellular processes) between affected and unaffected FTDP 17 brain regions and control brains using custommade cDNA macroarrays. The completion of these Aims will advance understanding of FTDP 17 and related tauopathies, and may provide new targets for diagnosis and therapeutics. -

Principal Investigator: VANCE, JEFFREY M
Grant Number: 2P50NS039764-06
Title: The Genetics of Parkinsonism

Abstract: This is a continuation application of our very successful Morris K. Udall Parkinson Disease Research Center of Excellence, seeking to identify genes that contribute to risk of developing PD. Four projects and two cores are proposed. Project I, "Candidate genes and complex interactions in PD," continues the association studies of potential susceptibility genes with PD, derived from biological candidates and the gene expression studies of Project II. Additional specific aims are gene-gene and environmental-gene interactions. Project II, "Expression Analysis and Genomic Convergence," continues and extends our expression studies of tissue obtained by our autopsy program by adding examination of the putamen and the anterior olfactory nucleus to the SN, as well as using Laser Capture Microscope to investigate specific cell types. Genes identified in project II will be tested for association in collaboration with Project I. Project III, "Mitochondrial genetics and PD," builds upon our finding of a highly significant association of mitochondrial-encoded proteins with PD, specifically the haplogroups J and K and SNP 10398, which lies in the complex I subunit ND3. Using cybrids, it looks for functional differences associated with these different mitochondrial haplogroups. It also will examine nuclear mitochondrial genes with significant differential expression in Project II for association with PD. Project IV, "Association Mapping in PD Linkage Regions," will identify PD genes in regions of linkage on chromosomes 5, 8, and 9 through a new approach, genomic "iterative" association mapping, using a new DNA pooling strategy. Once the strongest region of association is identified, haplotype-tagging will be utilized to fine map the region further. Genes lying in the region will be tested for association with PD. The projects depend heavily on our productive cores. In Core B we continue our very successful collection of PD patients and siblings, as well as our prospective autopsy program. Core C provides neuropathology support for investigation and diagnoses of autopsy material, brain banking and genotyping support for the projects. We believe that by utilizing these different but integrated approaches and resources we will be able to define the genetic contributions to PD. -

Principal Investigator: YOUNG, ANNE B
Grant Number: 2P50NS038372-06A1
Title: MGH/MIT MORRIS UDALL CENTER OF EXCELLENCE IN PD RESEARCH

Abstract: The MGH/MIT Morris Udall Center of Excellence in PD Research is taking a broad, collaborative and interactive approach to the study of Parkinson's disease. The Projects address critical questions concerning the selective vulnerability of dopamine neurons, the mechanism and consequences of Lewy body formation and alpha-synuclein aggregation, the neural systems consequences of parkinsonism and synuclein pathology, and molecular approaches for modifying this pathology. These issues will be explored using a range of systems, from yeast genetics, to mammalian cell culture, to rodent models to human postmortem material. The Center incorporates state-of-the-art technologies including high throughput yeast genetic screens to identify modifiers of synuclein aggregation and toxicity, viral vector gene transfer to study factors in mammalian cell culture and rodent models, multi-unit tetrode recordings to study striatal plasticity, fluorescence lifetime imaging to study protein-protein interactions, and laser capture microdissection and gene arrays to study transcriptional dysregulation. The Center has a Clinical and Training Core that provides care to patients with Parkinson's disease, gathers data on clinical features of the disease and response to therapy, solicits brain donations for neuropathological study, and trains outstanding clinician scientists to be future leaders in the field. The Center also has a Bioinformatics Core that serves to integrate and analyze data across the projects, and facilitate sharing of the information. The Administrative Core is charged with management of the Center and facilitating the sharing of information, ideas, and reagents among the investigators and with other components of the Udall Centers consortium. The investigators of the MGH/MIT Center are dedicated to a program of collaborative and interactive studies which will lead to better treatments for people with Parkinson's disease.-